

Amendments to the Claims:

This listing of claims will replace all prior versions of the claims in this application:

Listing of Claims:

Claims 1 - 222 (canceled)

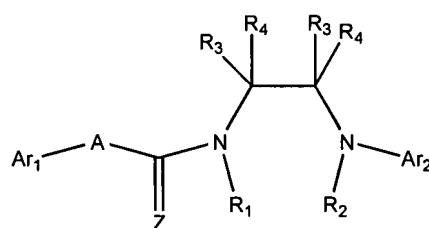
Claim 223 (currently amended): A method for treating pain in a mammal, the method comprising orally administering to the mammal a therapeutic dose of a capsaicin receptor antagonist that is not a capsaicin analogue wherein the antagonist, when tested in a human capsaicin receptor calcium mobilization assay employing a calcium sensitive fluorescent dye, produces a decrease of at least 80% compared to a matched control in the fluorescence response generated by capsaicin when: (i) the antagonist concentration is 1 micromolar and (ii) the capsaicin concentration is equal to capsaicin's EC₅₀ value for the assay.

Claim 224 (currently amended): A method according to claim 223, wherein the capsaicin receptor antagonist ~~is a high potency capsaicin receptor antagonist in an in vitro assay of capsaicin receptor antagonism~~ competes with resiniferatoxin in a capsaicin receptor binding assay and exhibits a K_i value in such an assay that is less than 100 nM.

Claim 225 (previously presented): A method according to claim 223, wherein the capsaicin receptor antagonist exhibits no detectable agonist activity in an in vitro assay of capsaicin receptor agonism.

Claim 226 (previously presented): A method according to claim 223, wherein a dose of the capsaicin receptor antagonist that is five times the minimum dose needed to provide analgesia in an adult mammalian laboratory animal, in an animal model for determining pain relief, does not cause sedation when administered to an adult mammalian laboratory animal in an animal model assay of sedation, wherein the same species is used in assessing analgesia and sedation.

Claim 227 (previously presented): A method according to claim 223 wherein the capsaicin receptor antagonist is a compound of the formula:



or a pharmaceutically acceptable salt thereof,

wherein:

A is absent or is selected from the group consisting of O, S, NR_A , $\text{CR}_B\text{R}_B'$, $\text{NR}_A\text{CR}_B\text{R}_B'$, $\text{CR}_B\text{R}_B'\text{NR}_A$, $-\text{CR}_A=\text{CR}_B-$, and C_3H_4 ; where R_A , R_B , and R_B' are independently selected at each occurrence from hydrogen or alkyl;

Z is oxygen or sulfur;

R_1 and R_2 independently represent hydrogen or alkyl;

R_3 and R_4 are independently selected at each occurrence from hydrogen; halogen; hydroxy; amino; cyano; nitro; $-\text{COOH}$; $-\text{CHO}$, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally

substituted $-S(O)_nNHalkyl$; optionally substituted $-S(O)_nN(alkyl)(alkyl)$; optionally substituted $-NHC(=O)alkyl$; optionally substituted $-NC(=O)(alkyl)(alkyl)$; optionally substituted $-NHS(O)_nalkyl$; optionally substituted $-NS(O)_n(alkyl)(alkyl)$; optionally substituted saturated or partially unsaturated heterocycloalkyl of from 5 to 8 atoms, which saturated or partially unsaturated heterocycloalkyl contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms independently selected from the N, O, and S;

or any two R_3 and R_4 not attached to the same carbon are taken together to form an optionally substituted aryl ring; an optionally substituted saturated or partially unsaturated carbocyclic ring of from 5 to 8 members; or an optionally substituted saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members that contains 1, 2, or 3 heteroatoms selected from N, O, and S; and

Ar_1 and Ar_2 are the same or different and independently represent optionally substituted cycloalkyl; an optionally substituted heterocycloalkyl ring of from 5 to 8 atoms that contains 1, 2, or 3 heteroatoms independently selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; or optionally substituted heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms independently selected from N, O, and S, and

n is independently chosen at each occurrence from 0, 1, and 2.

Claim 228 (previously presented): A method according to claim 223, wherein the pain is neuropathic pain.

Claim 229 (currently amended): A method according to claim 228, wherein the capsaicin receptor antagonist is a high-potency capsaicin receptor antagonist in an in

in vitro assay of capsaicin receptor antagonism competes with resiniferatoxin in a capsaicin receptor binding assay and exhibits a K_i value in such an assay that is less than 100 nM.

Claim 230 (previously presented): A method according to claim 228, wherein the capsaicin receptor antagonist exhibits no detectable agonist activity in an in vitro assay of capsaicin receptor agonism.

Claim 231 (previously presented): A method according to claim 228 wherein the neuropathic pain is associated with a condition selected from causalgia, neuritis, sciatic neuritis, peripheral neuritis, polyneuritis, optic neuritis, postfebrile neuritis, migrating neuritis, segmental neuritis, Gombault's neuritis, neuronitis, neuralgias, postherpetic neuralgia, trigeminal neuralgia, cervicobrachial neuralgia, cranial neuralgia, geniculate neuralgia, glossopharyngeal neuralgia, migranous neuralgia, idiopathic neuralgia, intercostals neuralgia, mammary neuralgia, mandibular joint neuralgia, Morton's neuralgia, nasociliary neuralgia, occipital neuralgia, red neuralgia, Sluder's neuralgia, splenopalatine neuralgia, supraorbital neuralgia, and vidian neuralgia.

Claim 232 (previously presented): A method according to claim 223, wherein the pain is peripheral nerve-mediated pain.

Claim 233 (previously presented): A method according to claim 223, wherein the pain is associated with a condition selected from postmastectomy pain syndrome, stump pain, phantom limb pain, oral neuropathic pain, Charcot's pain, toothache, venomous snake bite, spider bite, insect sting, postherpetic neuralgia, diabetic neuropathy, reflex sympathetic dystrophy, trigeminal neuralgia, osteoarthritis, rheumatoid arthritis, fibromyalgia, Guillain-Barre syndrome, meralgia paresthetica, burning-mouth syndrome, bilateral peripheral neuropathy, causalgia, sciatic neuritis, peripheral neuritis, polyneuritis, optic neuritis, postfebrile neuritis, migrating neuritis, segmental neuritis,

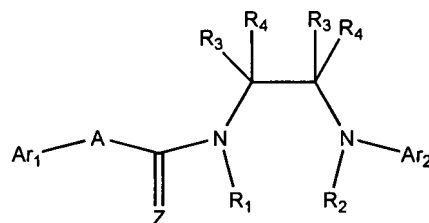
Gombault's neuritis, neuronitis, cervicobrachial neuralgia, cranial neuralgia, geniculate neuralgia, glossopharyngeal neuralgia, migranous neuralgia, idiopathic neuralgia, intercostals neuralgia, mammary neuralgia, mandibular joint neuralgia, Morton's neuralgia, nasociliary neuralgia, occipital neuralgia, red neuralgia, Sluder's neuralgia, splenopalatine neuralgia, supraorbital neuralgia, vidian neuralgia, sinus headache, tension headache, migraine headache, labor, childbirth, intestinal gas, menstruation, cancer, and trauma.

Claim 234 (previously presented): A method according to claim 223, where the pain is the result of exposure to capsaicin, exposure to heat, exposure to light, exposure to tear gas, hot peppers or pepper spray, or exposure to acid.

Claim 235 (previously presented): A method according to claim 234, wherein the capsaicin receptor antagonist exhibits no detectable agonist activity in an in vitro assay of capsaicin receptor agonism.

Claim 236 (previously presented): A method according to claim 234, wherein a dose of the capsaicin receptor antagonist that is five times the minimum dose needed to provide analgesia in an adult mammalian laboratory animal, in an animal model for determining pain relief, does not cause sedation when administered to an adult mammalian laboratory animal in an animal model assay of sedation, wherein the same species is used in assessing analgesia and sedation.

Claim 237 (previously presented): The method of claim 234 wherein the capsaicin receptor antagonist is a compound of the formula:



or a pharmaceutically acceptable salt thereof,

wherein:

A is absent or is selected from the group consisting of O, S, NR_A , $\text{CR}_B\text{R}_B'$, $\text{NR}_A\text{CR}_B\text{R}_B'$, $\text{CR}_B\text{R}_B'\text{NR}_A$, $-\text{CR}_A=\text{CR}_B-$, and C_3H_4 ; where R_A , R_B , and R_B' are independently selected at each occurrence from hydrogen or alkyl;

Z is oxygen or sulfur;

R_1 and R_2 independently represent hydrogen or alkyl;

R_3 and R_4 are independently selected at each occurrence from hydrogen; halogen; hydroxy; amino; cyano; nitro; $-\text{COOH}$; $-\text{CHO}$, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted $-\text{S}(\text{O})_n\text{NHalkyl}$; optionally substituted $-\text{S}(\text{O})_n\text{N(alkyl)(alkyl)}$; optionally substituted $-\text{NHC}(=\text{O})\text{alkyl}$; optionally substituted $-\text{NC}(=\text{O})(\text{alkyl})(\text{alkyl})$; optionally substituted $-\text{NHS}(\text{O})_n\text{alkyl}$; optionally substituted $-\text{NS}(\text{O})_n(\text{alkyl})(\text{alkyl})$; optionally substituted saturated or partially unsaturated heterocycloalkyl of from 5 to 8 atoms, which saturated or partially unsaturated heterocycloalkyl contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms independently selected from the N, O, and S;

or any two R₃ and R₄ not attached to the same carbon are taken together to form an optionally substituted aryl ring; an optionally substituted saturated or partially unsaturated carbocyclic ring of from 5 to 8 members; or an optionally substituted saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members that contains 1, 2, or 3 heteroatoms selected from N, O, and S; and Ar₁ and Ar₂ are the same or different and independently represent optionally substituted cycloalkyl; an optionally substituted heterocycloalkyl ring of from 5 to 8 atoms that contains 1, 2, or 3 heteroatoms independently selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; or optionally substituted heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms independently selected from N, O, and S, and n is independently chosen at each occurrence from 0, 1, and 2.